

### **Remarks**

Claims 127, 129 and 133 are pending in this application. Claims 128 and 130-132 are canceled in this paper without prejudice to Applicants' right to pursue the subject matter recited by them in one or more divisional, continuation, and/or continuation-in-part applications.

Claim 127 is amended to recite, in part, "optically pure (S,S)-2-(3-chlorophenyl)-3,5,5-trimethyl-3-morpholinol"<sup>1</sup> and "a selective serotonin reuptake inhibitor," each of which was recited by now canceled claims 128 and 132, respectively. Claim 129 is amended to remove the recitation of certain indications. New claim 133 is added to recite specific selective serotonin reuptake inhibitors. Support can be found, for example, on page 12, lines 7-19 of the specification. No new matter has been introduced.

#### **A. Applicants' Statement of Substance of Interview**

An in-person interview was held between the Examiner and Hoon Choi, Attorney for Applicants, on May 8, 2007. Applicants thank the Examiner for the courtesy she extended to Attorney for Applicants during the interview.

During the interview, the pending claims were discussed in view of the references cited by the Examiner. Attorney for Applicants pointed out that there is a teaching away with regard to the combination of optically pure (S,S)-hydroxybupropion and a selective serotonin reuptake inhibitor. The Examiner suggested that amended claims directed specifically to that combination be submitted, the suggestion to which Attorney for Applicants agreed.

#### **B. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn**

In the Office Action, the pending claims are rejected as allegedly obvious over U.S. Patent No. 6,274,579 to Morgan *et al.* ("Morgan"), in view of Spier *et al.*, *Depression and Anxiety*, 7: 73-75 (1998) ("Spier"). Furthermore, the claims are also rejected as allegedly obvious over U.S. Patent No. 6,677,678 to Howard

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<sup>1</sup> Please note that the chemical name has been amended (*i.e.*, (S,S)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol to (S,S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol) to remove any purported ambiguity in the chemical name originally recited by claim 128.

("Howard") or WO 99/17803 ("Cary"), in view of Morgan. Applicants respectfully traverse these rejections.

Although different combinations of references are used for the rejections, it appears that the rejections are essentially based on the Examiners allegation that the claims are obvious because: 1) Morgan allegedly discloses (S,S)-hydroxybupropion is an active metabolite of bupropion; and 2) other various references allegedly disclose the combination of bupropion and a selective serotonin reuptake inhibitor. Applicants respectfully disagree for at least the following reasons.

First, at the time of this application, it was well understood by those skilled in the art that each combination therapy should be assessed for its own merits. This is clearly evidenced by Post (a reference cited by the Examiner), which discloses, referring to combination therapies for bipolar depression, that "a panoply of treatment options now exist," and states that these potential therapies' "relative efficacy in different illness subtypes and stages remains to be better delineated, as do their optimal sequencing and use in combination in individual patients." (Post, page 184, under "Summary and Conclusion") (emphasis added).

In addition, Post states that when using combination therapies, "one has to be particularly careful about drug interactions and their potential for toxicity as well as therapeutic effects." (*Id.*). Post also teaches that "one should be aware of potential pharmacokinetic interactions" when using a combination therapy. (*Id.*). As can be seen from these statements, Post clearly teaches that no generalization can be made regarding any specific combination therapies for affective disorders. Consequently, the disclosure directed to the combination of bupropion and a selective serotonin reuptake inhibitor cannot provide a basis to conclude that the combination of (S,S)-hydroxybupropion and a selective serotonin reuptake inhibitor would have been obvious to those skilled in the art at the time of the invention.<sup>2</sup>

Second, and perhaps more importantly, Howard (also a reference cited by the Examiner), when read in view of Morgan, actually teaches those skilled in the art away from arriving at the claimed invention. This is because the portion of Howard relied on by the Examiner specifically discloses that "sexual dysfunction

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<sup>2</sup> This is more so considering that Morgan itself discloses that "the mechanism of action of bupropion, as with other antidepressants, is unknown." (Morgan, col. 1, lines 24-25). Therefore, Morgan certainly does not teach or suggest that (S,S)-hydroxybupropion can replace bupropion in its uses disclosed by the references cited by the Examiner.

associated with SSRI therapy can be reduced through the use of dopamine reuptake inhibitors, such as bupropion.” (*Id.*) (emphasis added). This clearly implies that the “advantage” in combining bupropion with SSRI therapy results from bupropion’s activity as a dopamine reuptake inhibitor.

Yet, Morgan discloses that (S,S)-hydroxybupropion is “approximately 10 fold less potent as an inhibitor of dopamine uptake” than racemic bupropion. (Morgan, col. 7, lines 26-28). Based on the disclosures of Howard and Morgan, those skilled in the art would not have been motivated to use (S,S)-hydroxybupropion, which has a much lower dopamine reuptake inhibitor activity, in the place of bupropion, which has a much higher dopamine reuptake inhibitor activity. Thus, Applicants respectfully submit that the presumption of obviousness established by the references cited by the Examiner, if any, would be rebutted in view of this teaching away.

Consequently, Applicants respectfully submit that the rejection of the claims under 35 U.S.C. § 103 should be withdrawn.

C. The Double Patenting Rejection Should Be Withdrawn

On pages 7-8 of the Office Action, the claims are provisionally rejected under judicially created non-statutory double patenting as allegedly unpatentable over the claims in the co-pending Application No. 09/987,930 (“the ‘930 application”) in view of Spier, Howard or Cary. Without addressing the substance of this rejection, Applicants respectfully request that this rejection be held in abeyance until the allowable subject matter in its final form is identified in this and the ‘930 application. Applicants will file a terminal disclaimer, if necessary, at an appropriate time.

Conclusion

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that rejections of the claims be withdrawn.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Date June 18, 2007

Respectfully submitted,

  
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